CLAIMS

What is claimed is:

1. A method for activating and expanding a population of T cells by cell surface moiety ligation, comprising:

a. providing a population of cells wherein at least a portion thereof comprises T cells;

b. contacting said population of cells with a surface, wherein said surface has attached thereto a first agent that ligates a first T cell surface moiety of a T cell, and the same or a second surface has attached thereto a second agent that ligates a second moiety of said T cell, wherein said ligation by the first and second agent induces proliferation of said T cell, and wherein said surface is present at a ratio of said surface to said cells such that at least one population of antigen-specific T cells is expanded at least about 10 fold in about 8 days.

2. The method of claim 1 wherein said ratio is from about 1:1 to about 1:100.

3. The method of claim 1 wherein said ratio is about 1:5.

4. The method of claim 1, wherein said same or a third surface has attached thereto a third agent that ligates a third moiety of said T cell wherein said ligation by the first, second, and third agents induces proliferation of said T cell.

5. The method of claim 4 wherein the third agent is an antibody or antibody fragment thereof.

6. The method of claim 5 wherein said third agent is an anti-4-1BB antibody or antibody fragment thereof.

7. The method of claim 1 at least one agent is an antibody or an antibody fragment.

8. The method of claim 7, wherein the first agent is an antibody or a fragment thereof, and the second agent is an antibody or a fragment thereof.

9. The method of claim 7, wherein the first and the second agents are different antibodies.

10. The method of claim 7, wherein the first agent is an anti-CD3 antibody, an anti-CD2 antibody, or an antibody fragment of an anti-CD3 or anti-CD2 antibody.

11. The method of claim 7, wherein the second agent is an anti-CD28 antibody or antibody fragment thereof.

12. The method of claim 7, wherein the first agent is an anti-CD3 antibody and the second agent is an anti-CD28 antibody.

13. The method of claim 12, wherein the anti-CD3 antibody and the anti-CD28 antibody are present at a ratio of about 1:1 to about 1:100.

14. The method of claim 1, wherein the first agent is an anti-CD3 antibody and the second agent is a ligand for CD28.

15. The method of claim 14, wherein the ligand is a natural ligand for CD28.

16. The method of claim 14, wherein the natural ligand is B7.

17. A population of T cells produced according to the method of any one of claims 1-16.

18. A method for the treatment of cancer comprising administering to a patient the population of T cells according to claim 17.

19. The method according to claim 18 wherein said cancer is selected from the group consisting of melanoma, non-Hodgkin's lymphoma, cutaneous T cell lymphoma, Hodgkin's disease, leukemia, plasmocytoma, sarcoma, glioma, thymoma, breast cancer, prostate cancer, colo-rectal cancer, kidney cancer, renal cell carcinoma, uterine cancer, pancreatic cancer, esophageal cancer, brain cancer, lung cancer, ovarian cancer, cervical cancer, testicular cancer, gastric cancer, esophageal cancer, multiple myeloma, hepatoma, acute lymphoblastic leukemia (ALL), acute myelogenous leukemia (AML), chronic myelogenous leukemia (CML), and chronic lymphocytic leukemia (CLL).

20. The method according to claim 18 wherein said cancer comprises multiple myeloma.

21. The method according to claim 18 wherein said cancer comprises CLL.

22. A method for activating and expanding a population of regulatory T cells by cell surface moiety ligation, comprising:

a. providing a population of cells wherein at least a portion thereof comprises regulatory T cells;

b. contacting said population of cells with a surface, wherein said surface has attached thereto a first agent that ligates a first T cell surface moiety of a regulatory T cell, and the same or a second surface has attached thereto a second agent that ligates a second moiety of said regulatory T cell, wherein said ligation by the first and second agent induces proliferation of said regulatory T cell.

23. The method according to claim 22 wherein the first agent is an anti-CD3 antibody and the second agent is an anti-CD28 antibody.

24. A composition comprising a population of T cells activated and expanded according to the following method:

a. providing a population of cells wherein at least a portion thereof comprises T cells;

b. contacting said population of cells with a surface, wherein said surface has attached thereto a first agent that ligates a first T cell surface moiety of a T cell, and the same or a second surface has attached thereto a second agent that ligates a second moiety of said T cell, wherein said ligation by the first and second agent induces proliferation of said T cell, thereby activating and expanding said population of T cells;

wherein said population of cells of part (a) is collected from a healthy individual for use at a later time point for the treatment of cancer in said individual.

25. A composition comprising a population of T cells according to any one of claims 1-16 and 22 wherein said population of cells wherein at least a portion thereof comprises T cells is collected from a healthy individual for use at a later time point for the treatment of cancer in said individual.

26. The composition of any one of claims 24-25 wherein said cancer is selected from the group consisting of melanoma, non-Hodgkin's lymphoma, cutaneous T cell lymphoma, Hodgkin's disease, leukemia, plasmocytoma, sarcoma, glioma, thymoma, breast cancer, prostate cancer, colo-rectal cancer, kidney cancer, renal cell carcinoma, uterine cancer, pancreatic cancer, esophageal cancer, brain cancer, lung cancer, ovarian cancer, cervical cancer, testicular cancer, gastric cancer, esophageal cancer, multiple myeloma, hepatoma, acute lymphoblastic leukemia (ALL), acute myelogenous leukemia (AML), chronic myelogenous leukemia (CML), and chronic lymphocytic leukemia (CLL).

27. The method according to claim 26 wherein said cancer comprises multiple myeloma.

28. The method according to claim 26 wherein said cancer comprises CLL.